Chapter 8: Pertussis

Dalya Guris, MD, MPH; Rebecca Martin, PhD; and Melinda Wharton, MD, MPH

I. Disease description

Pertussis, or whooping cough, is caused by the bacterium *Bordetella pertussis.* It is characterized by paroxysmal coughing followed by a characteristic inspiratory whoop. Secondary bacterial pneumonia is the cause of most pertussis-related deaths. Other complications, though infrequent, can include neurological complications such as seizures and encephalopathy, otitis media, and conditions resulting from the pressure effects of severe paroxysmal coughing including pneumothorax, epistaxis, subdural hematomas, hernias, and rectal prolapse. Disease rates and risk of serious complications, including death, are highest among young children, particularly those <1 year of age; disease in adolescents and adults tends to be milder.

Parapertussis, caused by the bacterium *B. parapertussis*, is similar to, although usually milder than, pertussis. Differentiation between pertussis and parapertussis is based on isolation of the organism in laboratory culture.

II. Background

In the early- to mid-1900s, pertussis was one of the most common childhood diseases and a major cause of childhood mortality in the United States. Since the introduction of pertussis vaccine in the 1940s, the average incidence of pertussis has decreased from 150 per 100,000 population between 1922 and 1940, to an average of 1.2 per 100,000 in the years 1980-1991.[1] However, since the 1980s, reported pertussis incidence has increased. The increase has been primarily in adolescents and adults, but reasons for the increase are not completely clear; improvements in diagnosis and reporting of pertussis in adolescents and adults appear to be important factors contributing to the overall increase.[2] In 1996, 7,796 cases were reported; this was the highest number of cases since 1976. In 1998, 7,133 cases of pertussis were provisionally reported. Since 1991, pertussis has emerged as the most frequently reported nationally notifiable vaccine-preventable disease among children <5 years of age.[3] Approximately 40% of reported pertussis cases are <5 years of age. In recent years, an increasing proportion of cases has been reported among adults, and the number of outbreaks reported among school-age children and adolescents has been increasing. Infected adolescents and adults may introduce pertussis into households where susceptible preschool-age children may be exposed.

III. Importance of rapid case identification

Early diagnosis and antimicrobial treatment of cases may lessen the severity of symptoms and may limit the period of communicability. In addition, prompt identification of cases may help identify un- or undervaccinated children among contacts. These children may be protected with vaccination. Antimicrobial prophylaxis of household and other close contacts may prevent secondary

cases. Because pertussis can be very severe among young infants, early antimicrobial prophylaxis is important in this age group.

IV. Importance of surveillance

Information obtained through surveillance is used to identify persons or areas in which additional efforts are required to reduce disease incidence. Surveillance data also help promptly identify outbreaks in which vaccination of un- or under-vaccinated children and antimicrobial prophylaxis of contacts can help limit the spread of disease. Effectiveness of outbreak control strategies is monitored by using surveillance data. Investigation of pertussis cases, including an analysis of vaccination status by age, can be used to determine whether the problem is predominantly failure to vaccinate or vaccine failure. Surveillance data also provide information that is used in evaluating vaccination policies at the state or national level. With licensure of multiple DTaP vaccines for use in infants, surveillance is even more important. Surveillance data will be used to monitor effectiveness of these new vaccines.

V. Disease reduction goals

For the year 2010, a disease reduction goal of 2000 indigenous cases of pertussis in children aged less than seven years has been proposed.[4]

VI. Case definitions

The following case definition for pertussis was approved by the Council of State and Territorial Epidemiologists (CSTE) in June 1997.[5]

Clinical case definition

A cough illness lasting at least 2 weeks with one of the following: paroxysms of coughing, inspiratory "whoop," or post-tussive vomiting, and without other apparent cause (as reported by a health professional).

Laboratory criteria for diagnosis

- Isolation of *B. pertussis* from a clinical specimen, or

- Positive polymerase chain (PCR) reaction assay for *B. pertussis*.

Case classification

Probable. Meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to a laboratory confirmed case.

Confirmed. 1) a person with an acute cough illness of any duration who is culture positive, or
2) a case that meets the clinical case definition and is confirmed by PCR, or

3) a case that meets the clinical definition and is epidemiologically linked directly to a case confirmed by either culture or PCR.

Comment. The clinical case definition is appropriate for endemic or sporadic cases. In outbreak settings, including household exposures, a case may be defined as a cough illness lasting ≥ 2 weeks. Occasionally, patients with an acute cough illness lasting <14 days but who are culture positive are detected as part of household investigations. Such cases should be reported as confirmed cases of pertussis. However, because PCR is less specific than culture, PCR positive cases with <14 days of cough should not be considered confirmed. Also due to this lack of specificity, outbreaks should be confirmed to be pertussis by positive culture results among several of the cases. For a case that meets the clinical case definition to be confirmed by epidemiologic linkage, the epidemiologic link must be directly to a case confirmed by either culture or PCR (i.e., a first generation contact).

The clinical case definition for pertussis was intended to provide increased sensitivity for detecting pertussis cases in situations where the disease was clinically compatible with pertussis but where confirmatory laboratory testing was negative (or not available). Among infants aged <6 months, apnea may occur and whoop or paroxysms may be absent. In young unvaccinated children, leukocytosis and lymphocytosis are common findings during the early paroxysmal stage.[6-8] Information on paroxysms of cough, whoop, and post-tussive vomiting should be routinely sought as part of case investigations. In an outbreak investigation in Missouri, a case definition of cough illness with whoop lasting ≥14 days was found to have a sensitivity of 81% and a specificity of 58%.[6] In other outbreaks in 1985 and 1986, a surveillance case definition of cough illness lasting for ≥14 days was found to be 84% sensitive and 63% specific for detecting culture-positive pertussis cases.[9] If it is not possible to collect information on paroxysms, whoop, and post-tussive vomiting, information on duration of cough (less than or ≥14 days) should be obtained in the course of the case investigation of each case of suspected pertussis. If the case investigation is done in the early stage of the disease, the case should be contacted later to determine if the duration of cough was at least 14 days.

Determining who has pertussis and who does not is often difficult, even in outbreaks. Whenever possible, all suspected cases of pertussis should have a nasopharyngeal swab or aspirate obtained for bacterial culture.

Studies have documented that direct fluorescent antibody testing (DFA) of nasopharyngeal secretions has low sensitivity (i.e., many persons who have pertussis test negative by DFA) and variable specificity (i.e., persons who don't have pertussis can test positive by DFA).[10, 11] For this reason, DFA should not be relied on as a criterion for laboratory confirmation. Serologic testing for pertussis is available in some areas but is not standardized and, therefore, should not be relied on as a criterion for laboratory confirmation for national reporting purposes. Both probable and confirmed cases should be reported to the National Notifiable Diseases Surveillance System (NNDSS).

VII. Laboratory testing

Determining who has pertussis and who does not is often difficult, even in outbreaks. Whenever possible, all suspected cases of pertussis should have a

nasopharyngeal swab or aspirate obtained for bacterial culture. Among household contacts of culture-confirmed cases, diagnosis of pertussis is usually based upon a characteristic history and physical examination. Laboratory tests may be particularly useful for sporadic cases or for young infants, and in all cases modified by prior vaccination, e.g., older children and adults.

A properly obtained nasopharyngeal swab or aspirate is essential for optimal results. Health department personnel who are asked to obtain these specimens should receive training and supervision from persons experienced in collection of nasopharyngeal specimens.

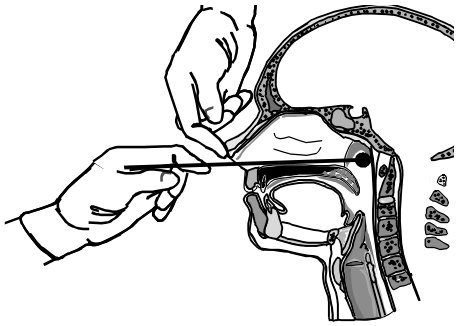
For additional information on use of the laboratory for support of vaccine-preventable disease surveillance, see Chapter 19.

Culture

The standard and preferred laboratory test for diagnosis of pertussis is isolation of *B. pertussis* by bacterial culture. Positive cultures are required to test for antimicrobial resistance and for molecular typing (e.g., pulse-field gel electrophoresis). Although bacterial culture is specific for the diagnosis, it is relatively insensitive. Under optimal conditions 80% of suspected cases in outbreak investigations can be confirmed by culture; in most clinical situations isolation rates are much lower.[12] The timing of specimen collection can affect the isolation rate, as can inadequately collected specimens.

Fastidious growth requirements make *B. pertussis* difficult to isolate. Isolation of the organism using direct plating is most successful during the catarrhal stage (i.e., first 1–2 weeks of cough). All suspected cases of pertussis should have a nasopharyngeal aspirate or swab obtained from the posterior nasopharynx for culture. For *B. pertussis*, nasopharyngeal aspirates have similar or higher rates of recovery than nasopharyngeal swabs[11, 13-15] throat and anterior nasal swabs have unacceptably low rates of recovery of *B. pertussis*. Therefore, specimens from the posterior nasopharynx (Figure), not the throat, should be obtained using Dacron® or calcium alginate swabs, not cotton, and should be plated directly onto selective culture medium or placed in transport medium. Regan-Lowe agar or freshly prepared Bordet-Gengou medium is generally used for culture; half-strength Regan-Lowe can be used as the transport medium. Success in isolating the organism declines with prior antibiotic therapy effective against pertussis (erythromycin or trimethoprim-sulfamethoxazole), delay in specimen collection beyond the first 3 weeks of illness, or in vaccinated individuals. A positive culture for *B. pertussis* confirms the diagnosis of pertussis. For this reason, access to a microbiology laboratory that can perform this service for no or for limited cost to the patient is a key component of pertussis surveillance.

Figure. Proper technique for obtaining a nasopharyngeal specimen for isolation of *B. pertussis*.



Direct fluorescent antibody testing (DFA)

DFA testing of nasopharyngeal secretions may be useful as a screening test for pertussis (a positive DFA result increases the probability that the patient truly has pertussis), but it is of limited specificity (frequent false-positive results) and should not be relied upon for confirmation of the diagnosis. A monoclonal DFA test recently became available (Accu-Mab ™, Biotex Laboratories, Inc., Edmonton, Canada). Initial evaluation demonstrated 65% sensitivity and 99% specificity when compared with culture.[16] Further testing is necessary to confirm these results.

A positive DFA result increases the probability that the patient truly has pertussis, but it is of limited specificity and should not be relied upon for confirmation.

Serologic testing

Although serological testing has proven useful in clinical studies, it is not yet standardized. Due to lack of association between antibody levels and immunity to pertussis, results of serologic testing are difficult to interpret. For these reasons, serologic testing is not widely available. In some areas it is used for clinical diagnosis and reporting,[17] but in the absence of standardization, serologic test results should not be relied upon for case confirmation for the purposes of national reporting. Cases meeting the clinical case definition that are serologically positive, but not culture positive or PCR positive, should be reported as probable cases.

Elevated white blood-cell count (WBC)

An elevated WBC with a lymphocytosis (i.e., increase in lymphocyte count) is usually present in cases of pertussis. The absolute lymphocyte count can reach $\geq$ 20,000/mm. However, there may be no lymphocytosis in very young infants, vaccinated children, or in mild cases of pertussis among adults. The white blood-cell count should not be used for confirmation.

Polymerase chain reaction (PCR)

PCR testing of nasopharyngeal swabs or aspirates is a rapid, sensitive, and specific method for diagnosing pertussis.[18] However, due to contamination in the laboratory or during specimen collection, false positive results may be obtained. PCR is currently available in some laboratories, and the assay varies among laboratories. Direct comparison with culture and serology is necessary for validation. Even if a laboratory has validated its PCR analysis, PCR should be used in addition to culture, because bacterial isolates may be required to evaluate antimicrobial resistance, and isolates are needed for molecular typing of strains circulating in the U.S.

Even if a laboratory has validated its PCR analysis, PCR should be used in addition to culture.

Pulsed-field gel electrophoresis (PFGE)

Pulsed-field gel electrophoresis (PFGE) is a type of DNA fingerprinting. This new technique has been a useful tool in distinguishing epidemiologically-related isolates (e.g., isolates from the same household or small community), while showing diversity within larger geographic areas such as cities, counties, and states.[19-21] Work is ongoing to standardize the technique in a few state laboratories. *B. pertussis* isolates, along with the clinical and epidemiological data for cases, are requested by the CDC Pertussis Laboratory to assist in this effort. For more information contact Dr. Gary Sanden at (404) 639-1238. Pertussis isolates should be sent to the Pertussis Laboratory (to the attention of Dr. Sanden), CDC, Room 5-240, MS C-O2, 1600 Clifton Road, Atlanta, GA 30333.

VIII. Reporting

Each state and territory has regulations and/or laws governing the reporting of diseases and conditions of public health importance (Appendix 2).[22] These regulations/laws list the diseases that are to be reported, and describe those persons or institutions responsible for reporting, including health-care providers, hospitals, laboratories, schools, day care facilities, and other institutions. Contact the state health department for reporting requirements in your state.

Reporting to CDC

Provisional reports should be sent to the National Notifiable Diseases Surveillance System by the state health department via the National Electronic Telecommunications System for Surveillance (NETSS). These data should be collected for each probable and confirmed case of pertussis; the Pertussis Surveillance Worksheet (Appendix 12) and the Pertussis Case Report Form (Appendix 13) may be used as guidelines in case investigation. Reporting should not be delayed because of incomplete information or lack of confirmation; following completion of case investigations, data previously submitted to NETSS should be updated with the available new information.

Most state health departments now access NETSS and input epidemiologically important information onto the supplementary pertussis screens. The screen

layout is similar to the Pertussis Case Report Form (Appendix 13). A few states continue to report this information in paper format to the Supplementary Pertussis Surveillance System (SPSS). These data, once entered into a computer data base at the CDC, are concatenated with NETSS data for analysis.

Information to collect

The following data are epidemiologically important and should be collected in the course of a case investigation. Additional information may be collected at the direction of the state health department.

- Demographic information

- Clinical data including
  - —Cough, date of cough onset, duration of cough
  - —Paroxysms, whoop, post-tussive vomiting, apnea

- Complications
  - —Pneumonia documented by chest x-ray
  - —Seizures
  - —Encephalopathy
  - —Hospitalization, number of days of hospitalization
  - —Death

- Treatment
  - —Antibiotic(s) used
  - —Duration of therapy

- Laboratory results
  - —Culture
  - —DFA
  - —Serology
  - —PCR

- Vaccine history
  - —Dates of administration of pertussis-containing vaccine
  - —Type of vaccine
  - —Manufacturer of vaccine
  - —Lot number
  - —Number of doses of pertussis-containing vaccine before illness onset
  - —Reason for non-vaccination

- Epidemiological information
  - —Date first reported to health department
  - —Date case investigation initiated
  - —Epidemiologic linkage to a laboratory confirmed case
  - —Association with an outbreak
  - —Transmission setting

—Setting outside household for further documented spread

It is important that information on the duration of cough be obtained, especially if the first interview is conducted within 14 days of cough onset and cough is still present.

• Contact investigation

It is important that information on the duration of cough be obtained, especially if the first interview is conducted within 14 days of cough onset and cough is still present. In these circumstances, a follow-up interview after 14 days of onset must be conducted to identify persons with cough duration $\geq$14 days. Because of the limitations of laboratory testing mentioned above, use of clinical case definitions is particularly important in the surveillance of pertussis.

The following definitions may be useful in pertussis case investigations.

Paroxysmal or spasmodic cough. Sudden uncontrollable "fits" or spells of coughing where one cough follows the next without a break for breath.

Whoop. High-pitched noise heard when breathing in after a coughing spasm.

Apnea. Prolonged breathlessness which may occur either after a coughing spasm, or spontaneously in an infant.

Cyanosis. Paleness or blueness of the skin, often most noticeable on the lips and tongue, occurring after coughing paroxysm.

Vomiting. Vomiting that follows a paroxysm of coughing (post-tussive vomiting).

Cold-like symptoms. Coryza (runny nose) or conjunctival injection (redness of the eyes) or both.

Positive chest x-ray for pneumonia. Evidence of acute pneumonia found on chest x-ray.

Acute encephalopathy. Acute illness of the brain manifesting as decreased level of consciousness (excluding transient drowsiness after a seizure), with or without seizures. Such patients are almost always hospitalized, and have undergone extensive diagnostic evaluations.

In addition, it is particularly important to collect details of vaccination (dates of each pertussis vaccination, type of vaccine, lot number, and manufacturer). Whole-cell pertussis vaccines are killed bacterial vaccines, provided in combination with diphtheria and tetanus toxoids as DTP or as DTP combined with *Haemophilus influenzae* type B conjugate vaccine (DTP-Hib). The first two combination diphtheria and tetanus toxoids and acellular pertussis vaccines (DTaP) were licensed in 1991 (ACEL - IMUNE®) and in 1992 (Tripedia®) for use as the first booster (fourth) and second booster (fifth) doses following three doses of whole-cell DTP. Since then, four DTaP vaccines have been licensed for use in infants (Tripedia®, ACEL-IMUNE®, Infanrix™ and

It is unknown if children receiving DTaP vaccines from different manufacturers will be optimally protected from pertussis. Thus, collection of all information related to vaccination history is important.

Certiva™). It is unknown if children receiving DTaP vaccines from different manufacturers will be optimally protected from pertussis. Thus, collection of all information related to vaccination history is important to monitor effectiveness of the pertussis vaccination program.

IX. Vaccination

Currently two types of pertussis vaccines combined with diphtheria and tetanus toxoids [i.e., acellular (DTaP) and whole-cell (DTP)] are available. The primary series of pertussis vaccination consists of a 3-dose series, with vaccine recommended at 2, 4, and 6 months of age. The fourth (first booster) dose is recommended at 15–18 months of age to maintain adequate immunity during preschool years. The fourth dose should be administered $\geq$6 months after the third. If the interval between the third and fourth doses is $\geq$6 months and the child is unlikely to return for a visit at the recommended age, the fourth dose of either DTaP or whole-cell DTP may be administered as early as age 12 months. The fifth (second booster) dose is recommended for children aged 4–6 years to confer continued protection against disease during the early school years. A fifth dose is not necessary if the fourth dose in the series is administered on or after the fourth birthday.[23]

Because of the lower frequency of adverse events, DTaP is preferred over whole-cell DTP.[23] All licensed DTaP vaccines are recommended for all five doses of the vaccination series. The vaccine safety and efficacy data are considered to be insufficient to select one acellular pertussis vaccine over another formulation.[24] Whole-cell DTP remains an acceptable alternative to DTaP when DTaP is not available.[25] For children who have started the vaccination series with one, two, three, or four doses of whole-cell DTP, DTaP is also recommended for all remaining doses in the schedule.

X. Enhancing surveillance

A number of surveillance activities can improve the detection and reporting of cases, and can improve the comprehensiveness and quality of reporting. Six states are conducting active laboratory-based surveillance for pertussis (Appendix 14). The following activities may be undertaken to enhance surveillance of pertussis. Chapter 16 lists additional activities for enhancing surveillance that may be applicable to pertussis surveillance.

Heightening the awareness of clinicians about pertussis, especially in adolescents and adults. Several recent studies suggest that pertussis is a common cause of cough illness of >7 days duration in adolescents and adults. [26] Because the disease is often atypical in presentation and many clinicians think of pertussis as a disease only of children, the diagnosis may not be considered. Cases among adolescents and adults are epidemiologically important because of their role in exposing infants and young children to pertussis.

Assuring that diagnostic testing for pertussis is being performed regularly. Unlike many of the other traditional vaccine-preventable diseases of

childhood, pertussis is an endemic disease in the United States. Pertussis cases are expected to occur in all communities, and several years with no reported cases from a jurisdiction may reflect failure of diagnosis or failure of reporting rather than a true absence of pertussis. The level of diagnostic testing being undertaken can be evaluated by reviewing the number of pertussis diagnostic tests (e.g., cultures) submitted by a jurisdiction.

Monitoring surveillance indicators. Regular monitoring of surveillance indicators may identify specific areas of the surveillance and reporting system that need improvement. Important indicators to evaluate thoroughness of case investigation and the timeliness of reporting of the surveillance system include:

- The proportion of probable and confirmed cases with complete information on vaccination history (dates of pertussis vaccine, pertussis vaccine type and manufacturer) and duration of cough.

- Median interval between onset of cough and notification of state or local public health authorities in probable and confirmed cases.

XI. Case investigation

Laboratory, hospital, and clinic records should be reviewed by health department personnel during case investigations in order to collect important information such as description of the clinical illness, outcome, immunization status, dates of vaccination, and vaccine lot numbers. The Pertussis Surveillance Worksheet (Appendix 12) and the Pertussis Report Form (Appendix 13) may be used as guidelines in conducting a case investigation.

Treatment and prophylaxis

The spread of pertussis can be limited by decreasing the infectivity of the patient and by protecting close contacts.[27] To reduce infectivity of a case as quickly as possible, a course of oral erythromycin in 4 divided doses for 14 days (children: 40 mg/kg/day; adults: 1 g/day) or trimethoprim-sulfamethoxazole in 2 divided doses for 14 days (children: trimethoprim 8 mg/kg/day, sulfamethoxazole 40 mg/kg/day; adults: trimethoprim 320 mg/day, sulfamethoxazole 1,600 mg/day) is recommended for patients with clinical pertussis. Antimicrobial therapy should be continued for 14 days to minimize any chance of treatment failure. The antibiotics and dosages used for chemoprophylaxis of contacts are the same as that recommended for treatment of a clinical case. For treatment and prophylaxis of pertussis, some physicians may choose to recommend use of other macrolides (e.g., azithromycin, clarithromycin). Treatment regimens with these antibiotics are simple and these newer agents may be better tolerated than erythromycin. However, data on efficacy of the new macrolides against pertussis disease are very limited and optimal duration of treatment is unknown.[28]

Prophylaxis of all household members and other close contacts may prevent or minimize transmission, although confirmatory data from controlled clinical trials are lacking. Non-household close contact may be described as a person who

has direct contact with respiratory secretions from the case (e.g., an explosive cough or sneeze in the face, sharing food, sharing eating utensils during a meal, kissing, mouth-to-mouth resuscitation, or conducting a full medical exam including examination of the nose and throat). Erythromycin or trimethoprim-sulfamethoxazole prophylaxis should be administered for 14 days to all household and other close contacts of persons with pertussis, regardless of age and vaccination status.[27]

Vaccination

All close contacts <7 years of age who have not received four doses of vaccine should complete the series with the minimal intervals (i.e., minimum age for first dose is 6 weeks; minimum intervals from dose one to two and from dose two to three are 4 weeks; minimum interval from dose three to four is 6 months). Close contacts <7 years of age who have received four doses of vaccine DTaP or whole-cell DTP but have not received a dose within 3 years of exposure should be given a booster dose of DTaP.

XII. Outbreak control

If cases are occurring among young infants, consideration should be given to lowering the age of vaccination of infants; the first dose of DTaP or whole-cell DTP can be given as early as 6 weeks of age, with a minimum interval of 4 weeks between each of the first 3 doses. However, implementation of an accelerated schedule might cause difficulties in achieving full coverage with other antigens.

Currently available pediatric formulations are not licensed for use among adults and should not be used for adults, even as half doses, due to the risk of adverse events from the higher diphtheria toxoid content of DTaP.

Adult formulations of acellular pertussis vaccine may be available in the future for outbreak control, but at present must be considered investigational (i.e., as part of a formal research study, approved by the appropriate institutional review board, and with informed consent of participants). Currently available pediatric formulations are not licensed for use among adults and should not be used for adults, even as half doses, due to the risk of adverse events from the higher diphtheria toxoid content of DTaP.

In school outbreaks, provision of antimicrobial prophylaxis to close classroom contacts of confirmed cases is recommended, but it is unclear under what conditions more aggressive school-wide prophylaxis should be administered.

During outbreaks, symptomatic persons should be considered contagious until 3 weeks after the onset of paroxysmal cough and should be excluded from school or day care until after receiving antimicrobial therapy for 5 days. Health-care workers with pertussis, or health-care workers who are symptomatic after exposure to a case, should be relieved from direct patient contact from the beginning of the catarrhal stage through the third week after onset of paroxysms, or until 5 days after the start of antimicrobial treatment. Some experts believe exclusion for 7 days is more appropriate for health care workers.[29, 30] A comprehensive document, *Guidelines for the Control of Pertussis Outbreaks* has been written to provide further guidelines for the control of pertussis outbreaks in households, schools and child care settings, hospitals,

institutions and clinics, and community settings, [31] and should be available by January, 2000. ❖

References

1. Davis SF, Strebel PM, Cochi SL, et al. Pertussis surveillance — United States, 1989-1991. MMWR 1992;41(SS-8):11-9.

2. Guris D, Strebel PM, Bardenheier B, et al. Changing epidemiology of pertussis in the United States: Increasing reported incidence among adolescents and adults, 1990-1996. Clin Infect Dis 1999;176:456-63.

3. CDC. Pertussis—United States, January 1992–June 1995. MMWR 1995;44:525-9.

4. United States Department of Health and Human Services. Office of Public Health and Science. Healthy People 2010 Objectives: Draft for Public Comment. Washington, D.C. September 15, 1999:22-9.

5. Council of State and Territorial Epidemiologists (CSTE). 1997 Position Statements. CSTE National Meeting, Saratoga Springs, NY; Position Statement ID 9.

6. Strebel PM, Cochi SL, Farizo KM, et al. Pertussis in Missouri: Evaluation of nasopharyngeal culture, direct fluorescent antibody testing, and clinical case definitions in the diagnosis of pertussis. Clin Infect Dis 1993;16:276-85.

7. Brooksaler F, Nelson JD. Pertussis: A reappraisal and report of 190 confirmed cases. Am J Dis Child 1967;114:389-96.

8. Heninger U, Cherry JD, Eckshardt T. Clinical and laboratory diagnosis of pertussis in the regions of a large vaccine efficacy trial in Germany. Ped Infect Dis J 1993;12:504-9.

9. Patriarca PA, Biellik RJ, Sanden G, et al. Sensitivity and specificity of clinical case definitions for pertussis. Am J Public Health 1988;78: 833-6.

10. Broome CV, Fraser DW, English WJ. Pertussis. Diagnostic methods and surveillance. In: Manclark CR, Hill JC, eds. International symposium on pertussis. National Institutes of Health: Bethesda, MD, 1978;19-22.

11. Halperin SA, Bartolussi R, Wort AJ. Evaluation of culture, immunofluorescence and serology for the diagnosis of pertussis. J Clin Microbiol 1989;27:752-7.

12. Onorato MI, Wassilak SGF. Laboratory diagnosis of pertussis: The state of the art. Pediatr Infect Dis J 1987;6:145-51.

13. Bejuk J, Begovac J, Bace A, et al. Culture of *Bordetella pertussis* from three upper respiratory tract specimens. Ped Infect Dis J 1995;14:64-5.

14. Hallander HO, Reizenstein E, Renemar B, et al. Comparison of nasopharyngeal aspirates with swabs for culture of *Bordetella pertussis*. J Clin Microbiol 1993;31:50-2.

15. Hoppe JE, Weiss A. Recovery of *Bordetella pertussis* from four kinds of swabs. Euro J Clin Microbiol 1987;6:203-5.

16. McNicol P, Giercke SM, Gray M, et al. Evaluation and validation of a monoclonal immunofluorescent reagent for direct detection of *Bordetella pertussis*. J Clin Microbiol 1995;33:2868-71.

17. Marchant CD, Loughlin AM, Lett SM, et al. Pertussis in Massachusetts, 1981-1991: Incidence, serologic diagnosis, and vaccine effectiveness. J Infect Dis 1994;169:1297-1305.

18. Meade BD, Bollen A. Recommendations for use of the polymerase chain reaction in the diagnosis of *Bordetella pertussis* infections. J Med Microbiol 1994;41:51-5.

19. Khattak MN, Matthews RC, Burnie JP. Is *Bordetella pertussis* clonal? Brit Med J 1992;302:813-5.

20. Khattak MN, Matthews RC. Genetic relatedeness of *Bordetella pertussis* species as determined by macrorestriction digests resolved by pulsed-field gel electrophoresis. Int J Syst Bacteriol 1993;43:659-64.

21. De Moissac YR, Ronald SL, Peppler MS. Use of pulsed-field gel electrophoresis for epidemiological study of *Bordetella pertussis* in a whooping cough outbreak. J Clin Microbiol 1994;32:398-402.

22. Roush S, Birkhead G, Koo D, et al. Mandatory reporting of diseases and conditions by health care professionals and laboratories. JAMA 1999;282:164-70.

23. CDC. Pertussis vaccination: use of acellular pertussis vaccines among infants and young children - recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1997;46 (RR-7):1-25.

24. CDC. Notice to Readers. FDA Approval of a Fourth Acellular Pertussis Vaccine for Use Among Infants and Young Children. MMWR 1998; 47(43);934-36.

25. CDC. Notice to Readers. Recommended Childhood Immunization Schedule - United States, 1999. MMWR 1999;48(1);12-6.

26. Nennig ME, Shinefield HR, Edwards KM, et al. Prevalence and incidence of adult pertussis in an urban population. JAMA 1996;275:1672-4.

27. American Academy of Pediatrics. Pertussis. In: Peter G, ed. 1997 Red Book: Report of the Committee on Infectious Diseases. 24th ed. American Academy of Pediatrics: Elk Grove Village, IL 1997;394-407.

28. Aoyama T, Sunakawa K, Iwata S, et al. Efficacy of short-term treatment of pertussis with clarithromycin and azithromycin. J Pediatr 1996;129:761-4.

29. Williams WW. Guidelines for infection control in hospital personnel. Infect Control 1983;4(suppl):326-49.

30. Strebel P, Pertussis. In: APIC Infection Control and Applied Epidemiology. St. Louis: Mosby, 1996:71(1):71-5.

31. CDC. Guidelines for the control of pertussis outbreaks. Centers for Disease Control and Prevention: Atlanta, GA. In press.